STATEMENT OF WORK FOR UNIVERSITY OF PENNSYLVANIA

Title – Restoring Active Memory (RAM): "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)

1.0 SCOPE

This effort promises to use direct brain recordings and stimulation in humans and animals to create a real-time system for enhancing encoding and long-term retrieval of memories for specific types of information. The team consists of nine leading clinical centers for the surgical treatment of epilepsy and movement disorders, each led by a clinician scientist with substantial experience in one or more key areas of electrical brain stimulation, human cognition, computational electrophysiology, and realtime adaptive control systems. The neurological and neurosurgical teams are aligned on the common goal of rapidly developing and testing approaches to enhance and restore memory through a study of unprecedented scope: more than 100 patients each year in a large array of experiments. Pending Investigational Device Exemption (IDE) approval, patients in Phase 2 of the project will be implanted with a complete memory neuromodulation (b)(4) to our memory testing paradigms. This will be accomplished through an accelerated U.S. Food and Drug Administration (FDA) submission of the technical area two (TA2) system at the end of Phase 1. Through application of a computational model of human (b)(4) to the behavioral and electrophysiological data the recipient shall define biomarkers of memory (b)(4) These biomarkers will be used (b)(4) (b)(4)

1.1. BACKGROUND

The Defense Advanced Research Projects Agency (DARPA) seeks new methods for analysis and decoding of neural signals in order to understand how neural stimulation could be applied to facilitate recovery of memory encoding following brain injury. Ultimately, it is desired that a prototype implantable neural device that enables recovery of memory in a human clinical population be developed. Additionally, the program encompasses the development of quantitative models of complex, hierarchical memories and exploration of neurobiological and behavioral distinctions between memory function using the implantable device versus natural learning and training.

2.0 APPLICABLE DOCUMENTS

(a) DARPA BAA-14-08.

(b) UPENN Technical Proposal Titled "Memory Enhancement with Modeling, Electrophysiology, and Stimulation (MEMES)" dated January 23, 2014

3.0 PROJECT WORK DESCRIPTION AND REQUIREMENTS

The recipient shall provide the facilities necessary to develop the effort as described herein.

Human use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Review Board (IRB) approvals, show proper assurance documentation, and obtain proper approval from the Government officials prior to human use testing.

Animal use **is** anticipated in this effort. The recipient shall obtain all necessary Institutional Animal Care and Utilization Committee (IACUC) approval and demonstrate this approval to the Government prior to beginning experimentation with animals. If animal use is no longer anticipated, or changes significantly from the approved

IACUC then the PI must submit a letter stating the discontinuation of animal use for this effort and/or receive appropriate authorization for IACUC changes of previously specified protocols. Unless prior approval by DARPA is given IACUC documentation must be provided prior to contract award.

3.1 BASE PERIOD (PHASE I)

Technical Area 1

3.1.1 A computational model for describing behavior in declarative memory tasks.

3.1.1.1 Predicting moment-by-moment behavior in a variety of memory tasks.
The recipient shall document a model of memory (b)(4) .

(a) The recipient shall document the code base for the (b)(4) [Month 3].

(b) The recipient shall extend the model (b)(4) [Month 6].

(c) The recipient shall document fully commented, optimized (b)(4) Code shall be able to execute model (b)(4) [Month 6].

(d) The recipient shall document the code base for the (b)(4) (b)(4) [Month 9].

(e) The recipient shall fit the (b)(4) [Month 12].

(f) The recipient shall document fully commented, optimized (b)(4) Code shall be able to execute model (b)(4) [Month 12].

3.1.1.2 [DELETED]

3.1.1.3. Build a (b)(4) model of free recall: (b)(4)

(a) Develop software that allows us to construct the (b)(4) model for an entire session of FR1 in 30 seconds or less [Month 15]

(b) [DELETED]

(c) [DELETED]

3.1.1.4 Build a (b)(4) model for (b)(4) memory: (b)(4)

(b)(4)

(a) Develop a model prototype (b)(4) [Month 21]

(b) Deliver fully documented code (b)(4) [Month 24]

3.1.2 Integrating neurophysiological biomarkers into the computational model of behavior.

3.1.2.1 Characterize distribution of (b)(4) biomarkers (b)(4)

3.1.2.1.1 A prototype for analyzing (b)(4) neural (b)(4) shall be deployed and evaluated [Month 12].

3.1.2.1.2 The recipient shall document the prototype software (b)(4) [Month 12].

3.1.2.1.3 Characterize the (b)(4) biomarkers using the models of free recall and (b)(4) navigation:

(a) Characterize the (b)(4) biomarkers for patients performing the free recall task, (b)(4) [Month 18].

(b) Characterize the (b)(4) biomarkers for patients performing the (b)(4) navigation task, (b)(4) [Month 24].

3.1.2.1.4 The recipient shall document the prototype software (b)(4) (b)(4) The recipient shall document the software used (b)(4) (b)(4) [Month 24].

3.1.3 Electrophysiological recordings to define biomarkers (b)(4) memory.

Objective: Define biomarkers (b)(4) memories, as measured in a broad array of tasks. The subtask list that follows references the following experiments: (b)(4) free recall of (b)(4) word lists (FR), (b)(4) free recall (b)(4)FR), spatial navigation (b)(4) (b)(4), and paired associate learning (PAL).

3.1.3.1 The recipient shall design, program, pilot, execute, and analyze data from Experiment FR1 on patients in the epilepsy monitoring unit. Recording neural activity (b)(4) shall be used to identify (b)(4) biomarkers (b)(4) of (b)(4) memory (b)(4) These biomarkers will serve a critical role in subsequent (b)(4) experiments. The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 13 patients from experiment FR1 [Month 8].
(d) Analyze data on 26 patients from experiment FR1 [Month 13].
(e) Analyze data on 39 patients from experiment FR1 [Month 18].
(f) Analyze data on 58 patients from experiment FR1 [Month 24].

(g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (neuroradiology) and carry out 3D reconstructions (b)(4) [Month 24].

(h) Complete interim reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, (b)(4) as well as analyses of the electrophysiological correlates of (b)(4) memory (b)(4) [Month 24].

(i) Post all data collected in a deidentified format compatible with the public data portal [Month 24].

(j) Fully document code for experiment [Month 2].

(k) Fully document analysis functions [Month 3].

(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].

(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].

(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

(o) Deliver report on (b)(4) biomarkers [Month 24].

3.1.3.2 Design, program, pilot, execute, and analyze data from Experiment CatFR1 (n=46) on patients in the epilepsy monitoring unit. In this task the recipient shall define biomarkers of (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].

(b) Write initial data analysis scripts [Month 3].

(c) Analyze data on 11 patients from experiment CatFR1 [Month 8].

(d) Analyze data on 23 patients from experiment CatFR1 [Month 13].

(e) Analyze data on 28 patients from experiment CatFR1 [Month 18].

(f) Analyze data on 33 patients from experiment CatFR1 [Month 24].

(g) Organize and annotate patient data from above experiment [Month 24].

(h) Complete interim reports on data from the above experiment [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].

(j) Fully document code for experiment [Month 2].

(k) Fully document analysis functions [Month 3].

(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].

(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].

(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

(o) Deliver report on (b)(4) biomarkers [Month 24].

3.1.3.3 Design, program, pilot, execute, and analyze data from Experiment YC1 (n=44) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers of (b)(4) memory (b)(4) . The recipient shall identify (b)(4) memory biomarkers, (b)(4) as well as (b)(4) memory biomarkers, (b)(4) (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].

(b) Write initial data analysis scripts [Month 3]

(c) Analyze data on 11 patients from experiment YC1 [Month 8].

(d) Analyze data on 22 patients from experiment YC1 [Month 13].

(e) Analyze data on 33 patients from experiment YC1 [Month 18].

(f) Analyze data on 50 patients from experiment YC1 [Month 24].

(g) Organize and annotate patient data from above experiment [Month 24].

(h) Complete interim reports on data from the above experiment [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].

(j) Fully document code for experiment [Month 2].

(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].
(o) Deliver report on (b)(4) biomarkers [Month 24].

3.1.3.4 Design, program, pilot, execute, and analyze data from Experiment PAL1 (n=30) on patients in the epilepsy monitoring unit. In this task the recipient shall identify biomarkers (b)(4) of (b)(4) associations and shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 7 patients from experiment PAL1 [Month 8].
(d) Analyze data on 14 patients from experiment PAL1 [Month 13].
(e) Analyze data on 22 patients from experiment PAL1 [Month 18].
(f) Analyze data on 25 patients from experiment PAL1 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete interim reports on data from the above experiment [(Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide interim reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].
(o) Deliver report on (b)(4) biomarkers [Month 24].

3.1.3.5 Design, program, pilot, execute and analyze data from Experiment DBS2 (n=20) on patients undergoing DBS for movement disorders and Parkinson's Disease. In this task the recipient shall perform a (b)(4) recall task (see (b)(4) Recall Task, above). (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 4 patients from experiment DBS2 [Month 8].
(d)-(n) [DELETED]

3.1.4 Stimulation to (b)(4) memory

3.1.4.1 Design, program, pilot, execute, and analyze data from Experiment FR2 (n=18). The recipient shall test the hypothesis (b)(4) The recipient shall compare the degree to which (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 4 patients from experiment FR2 [Month 8].
(d) Analyze data on 8 patients from experiment FR2 [Month 13].
(e) Analyze data on 13 patients from experiment FR2[Month 18].
(f) Analyze data on 43 patients from experiment FR2 [Month 24].
(g) Organize and annotate patient data from the above experiment to be shared with investigators and program personnel; precisely localize electrode contacts (b)(4) carry out 3D reconstructions (b)(4) (b)(4) [Month 24].

(h) Complete final reports on data from the above experiment to be presented at team meetings and with DARPA program personnel. Reports shall include detailed analyses of behavioral data, (b)(4) (b)(4), as well as analyses of the electrophysiological correlates of (b)(4) memory (b)(4) [Month 24].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].

(j) Fully document code for experiment [Month 2].

(k) Fully document analysis functions [Month 3].

(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].

(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].

(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].

(o) Expand analysis functions (b)(4). Deliver updated and fully documented analysis code [Month 7].

3.1.4.2 Design, program, pilot, execute, and analyze data from Experiment FR3 (n=18). The recipient shall test (b)(4) (b)(4) and shall:

(a) Design, program, and pilot task [Month 12].

(b) Write initial data analysis scripts [Month 13].

(c) Analyze data on 4 patients from experiment FR3 [Month 14].

(d) [DELETED]

(e) Analyze data on 10 patients from experiment FR3 [Month 24].

(f) Analyze data on 18 patients from experiment FR3 [Month 30].

(g) Organize and annotate patient data from above experiment [Month 30].

(h) Complete final reports on data from the above experiment [Month 30].

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 30].

(j) Fully document code for experiment [Month 12].

(k) Fully document analysis functions [Month 13].

(l) [DELETED]

(m) [DELETED]

(n) [DELETED]

(o) Expand analysis functions (b)(4) Deliver updated and fully documented analysis code [Month 13].

3.1.4.3 [DELETED]

3.1.4.4 Design, program, pilot, execute, and analyze data from Experiment CatFR2. (b)(4) Further, the recipient (b)(4) nd shall:

(a) Design, program, and pilot task [Month 2].

(b) Write initial data analysis scripts [Month 3].

(c) Analyze data on 4 patients from experiment CatFR2 [Month 8].

(d) Analyze data on 8 patients from experiment CatFR2 [Month 13].

(e) Analyze data on 13 patients from experiment CatFR2 [Month 18].

(f) Analyze data on 18 patients from experiment CatFR2 [Month 24].

(g) Organize and annotate patient data from above [Month 24].

(h) Complete final reports on data from the above experiment [Month 24]

(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24]

(j) Fully document code for experiment [Month 2].

(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].
(n) Expand analysis functions (b)(4) Deliver updated and fully documented analysis code [Month 7].

3.1.4.5 Design, program, pilot, execute, and analyze data from Experiment CatFR3. In CatFR3 the recipient shall test the ability (b)(4) (b)(4) . The recipient shall:

(a) Design, program, and pilot task [Month 12].
(b) Write initial data analysis scripts [Month 13].
(c) Analyze data on 4 patients from experiment CatFR3 [Month 24].
(d) Analyze data on 8 patients from experiment CatFR3 [Month 30].
(e) [DELETE]
(f) [DELETE]
(g) [DELETE]
(h) [DELETE]
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 30].
(j) Fully document code for experiment [Month 12].
(k) Fully document analysis functions [Month 13].
(l) [DELETE]
(m) [DELETE]
(n) [DELETE]
(o) Expand analysis functions (b)(4) Deliver updated and fully documented analysis code [Month 13].

3.1.4.6 Design, program, pilot, execute, and analyze data from Experiment YC2. The recipient shall apply (b)(4) stimulation (b)(4) The recipient shall test the ability of stimulation to improve memory (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 5 patients from experiment YC2 [Month 8].
(d) Analyze data on 10 patients from experiment YC2 [Month 13].
(e) Analyze data on 16 patients from experiment YC2 [Month 18].
(f) Analyze data on 33 patients from experiment YC2 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24]
(n) Post annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].
(o) Expand analysis functions (b)(4) Deliver updated and fully documented

analysis code [Month 7].

3.1.4.7 [DELETED]

3.1.4.8 Design, program, pilot, execute, and analyze data from Experiment PAL2. (b)(4) The recipient shall (b)(4)

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 3 patients from experiment PAL2 [Month 8].
(d) Analyze data on 6 patients from experiment PAL2 [Month 13].
(e) Analyze data on 9 patients from experiment PAL2 [Month 18].
(f) Analyze data on 11 patients from experiment PAL2 [Month 24].
(g) Organize and annotate patient data from above experiment [Month 24].
(h) Complete final reports on data from the above experiment [Month 24].
(i) Post all data collected so far in a deidentified format compatible with the public data portal [Month 24].
(j) Fully document code for experiment [Month 2].
(k) Fully document analysis functions [Month 3].
(l) Create 3D reconstructions of all patients run in the task in Phase 1 [Month 24].
(m) Provide final reporting on analyzed data from all patients run in the task in Phase 1 [Month 24].
(n) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 24].
(o) Expand analysis functions (b)(4) (b)(4) Deliver updated and fully documented analysis code [Month 7].

3.1.4.9 Design, program, pilot, execute, and analyze data from Experiment PAL3. (b)(4) The recipient shall:

(a) Design, program, and pilot task [Month 12].
(b) Write initial data analysis scripts [Month 13].
(c) [DELETED]
(d) [DELETED]
(e) Analyze data on 4 patients from experiment PAL3 [Month 24].
(f) Analyze data on 8 patients from experiment PAL3 [Month 30].
(g) [DELETED]
(h) [DELETED]
(i) [DELETED]
(j) Fully document code for experiment [Month 12].
(k) Fully document analysis functions, (b)(4) [Month 13].
(l) [DELETED]
(m) [DELETED]
(n) [DELETED]
(o) Expand analysis functions (b)(4) Deliver updated and fully documented analysis code [Month 13].

3.1.4.10 Design, program, pilot, execute and analyze data from Experiment DBS1.
The recipient shall evaluate (b)(4) for (b)(4) learning during

a (b)(4) task. (b)(4) (b)(4) The recipient shall vary (b)(4) parameters. (b)(4) The recipient shall index learning (b)(4) The recipient shall compare (b)(4) cross the five conditions (b)(4) (b)(4) and (2) identify (b)(4) parameters (b)(4) and shall:

(a) Design, program, and pilot task [Month 2].
(b) Write initial data analysis scripts [Month 3].
(c) Analyze data on 10 patients from experiment DBS1 [Month 8].
(d) – (n) [DELETED]

3.1.4.11 Design, program, execute, and analyze data from Experiments PS1, PS2 & PS3. The recipient shall (b)(4) (b)(4) identify (b)(4) stimulation parameters:

(a) Design and program tasks [Month 12].
(b) Analyze data on 14 patients each from experiments PS1, PS2, & PS3 [Month 16].
(c) Analyze data on 29 patients each from experiments PS1, PS2, & PS3 [Month 24].
(d) Post fully annotated data to the public data portal for all patients run in the task in Phase 1 [Month 30].

3.1.5 Develop control algorithms (b)(4).

3.1.5.1 [DELETED]

3.1.5.2 Develop algorithms (b)(4) The recipient shall:

(a) Complete interim report (b)(4) [Month 9].
(b) Develop prototype (b)(4) Complete 12-month interim report on algorithms, (b)(4) (b)(4). [Month 12].
(c) [DELETED]
(d) [DELETED]
(e) Provide 9-month interim report on (b)(4) algorithms [Month 9].
(f) Provide 12-month interim report on (b)(4) algorithms [Month 12].
(g) Document 12-month prototype (b)(4) algorithms [Month 12] .
(h) [DELETED]
(i) [DELETED]
(j) [DELETED]
(k) [DELETED]

3.1.5.3 [DELETED]

3.1.5.4 [DELETED]

3.1.6 Core project resources devoted to TA1.

3.1.6.1 The recipient shall perform electrophysiological experiment development and programming, data analysis, computational cluster effort towards data analysis and computational modeling from TA1.

3.1.6.2 The recipient shall provide project coordination, data sharing and data storage.

3.1.7 Determine electrode requirements for (b)(4) stimulation in Phase 2. The recipient shall characterize (b)(4) for modulating and restoring memory function.

3.1.7.1 The recipient shall design and develop an electrode (b)(4) (b)(4) capable (b)(4) (b)(4). The recipient shall:

(a) Based on precise anatomical analyses (b)(4) (b)(4) [Month 12].

(b) Working with Lawrence Livermore National Labs (LLNL), deliver a formal technical drawing and list of materials that can be put into place by the beginning of Phase 2 [Month 18].

(c) Working with LLNL, complete ISO-10993 testing to verify lead biocompatibility and stability, and submit the design history file and associated ISO test results required for IDE submission to the FDA [Month 29].

(d) [DELETED]

3.1.8 [DELETED]

3.1.9 [DELETED]

Technical Area 2

3.1.10 Validate system architecture and individual components. The recipient shall document and review the high-level system design requirements against current design assumptions.

3.1.10.1 The recipient shall validate system level specification with TA1 team [Months 1–6].

3.1.10.2 [DELETED]

3.1.10.3 The recipient shall refine the specifications for electronics (b)(4) (b)(4), continually refining as needed [Months 4–9].

3.1.10.4 The recipient shall validate the specification for the Algorithm prototyping system and user interface [Months 5–6].

3.1.10.5 The recipient shall define the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Month 6] and shall:

(a) Document definitions of the functional, operation, and performance requirements of the overall system [Month 6].

(b) Document definitions of the component-level specifications for the neural interface, electronics, external packaging, and algorithm prototyping system [Month 9].

(c) Document definitions of the sub-chronic safety and performance data required by the FDA for the 29-day IDE approval [Month 6]

(d) Deliver definitions of stakeholder requirements [Month 4]

3.1.11 Design, fabrication, and characterization of the external neuromodulation stimulator. The recipient shall develop a (b)(4) capable of mating with (b)(4) (b)(4)electrodes. (*and any adaptations needed to ensure adequate clinical care.)

3.1.11.1 The recipient shall design and manufacture of electronics, (b)(4) Months 7–18].

3.1.11.2 The recipient shall (b)(4) software (firmware) to control the electronics and provide (b)(4) (b)(4)

capability [Months 7–18].

3.1.11.3 The recipient shall modify design and manufacture the mechanical connecto (b)(4) (b)(4) o interface with the clinical depth electrodes and cortical/subcortical grids/strips [Months 7–18].

3.1.11.4 The recipient shall manufacture, test, document safety and performance testing, and delive (b)(4) in preparation for FDA IDE submission and system delivery to clinical sites [Months 19–24].

(a) Design and build electronics, (b)(4) [Months 7-18].
(b) Document the (b)(4) software that controls the electronics and documen (b)(4) algorithm capability [Month 18].
(c) Modify the design of the mechanical connector and build 22 (b)(4) for design verification testing [Month18].
(d) Test and document safety and performance (b)(4) in preparation for FDA IDE submission [Month 24].

3.1.12 Connectorization and Integration of electrode arrays with (b)(4) timulator. The recipient shall develop a connectorization method and integrate a variety of clinical electrode designs with the Medtroni (b)(4) neural stimulator.

3.1.12.1 The recipient shall define specifications for the connector (b)(4) [Months 1–6].

3.1.12.2 [DELETED]

3.1.12.3 [DELETED]

3.1.12.4 The recipient shall design verification testing to ensure electrical conductivity and reliability, moisture resistance, mechanical integrity [Months 15–24]. The recipient shall:

(a) Define specifications for the connector [Month 6].
(b) [DELETED]
(c) Document the assembly process (b)(4) [Month 15].
(d) Complete and document connector Prototype [Month 15].
(e) Design verification testing to ensure electrical conductivity and reliability, and mechanical integrity [Month 24].

3.1.13 Algorithm prototyping system. The recipient shall develop an algorithm prototypin (b)(4) (b)(4)

3.1.13.1 The recipient shall design (b)(4) interface (b)(4) [Months 1–6].

3.1.13.2 The recipient shall document the software used (b)(4) [Months 1–12].

3.1.13.3 The recipient shall develop software (b)(4) [Months 7–18].

3.1.13.4 The recipient shall verify and validate testing and documentation for IDE submission [Months 19–24]. The recipient shall:

(a) Design (b)(4) interface t

(b)(4) Month 6].

(b) Document the software used (b)(4) [Month 12].

(c) Document the software (b)(4) [Month 18].

(d) Complete prototype software package [Month 18].

(e) Verify and validate testing and documentation for IDE submission [Month 24].

3.1.14 System verification and validation testing. The recipient shall evaluate and verify system lifetime, sterility and biocompatibility. The recipient shall also verify and validate the system functions and interfaces (b)(4) (b)(4) (b)(4) Additionally, system verification and validation shall be performed.

3.1.14.1 [DELETED]

3.1.14.2 [DELETED]

3.1.14.3 [DELETED]

3.1.14.4 The recipient shall perform (b)(4) system verification testing for sub-chronic (< 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Months 19–24].

3.1.14.5 The recipient shall validate the (b)(4) system [Month 19–24]. The recipient shall:

(a) Fabricate and assemble fully-integrated systems for testing [Month 18].

(b) [DELETED]

(c) [DELETED]

(d) [DELETED]

(e) Report on electronics testing for sub-chronic (< 29-days) use as outlined in ANSI / AAMI / ISO 14971:2007/(R)2010 [Month 24].

(f) [DELETED]

(g) Validate and fully document a system that is ready for FDA IDE submission; deliver system verification and validation reports [Month 24].

3.1.15 [DELETED]

3.1.16 (b)(4) Electrode Design.

3.1.16.1 The recipient shall deliver development plans for a novel (b)(4) lead suitable for interfacing with the (b)(4) device. The recipient shall:

(a) Identify at least one partner capable of delivering the electrode [Month 7]

(b) Deliver a technical drawing, estimated development and manufacturing budget, and identify any cost sharing activities [Month 7]

Technical Area 3

The recipient shall perform basic research findings (b)(4) to inform the human stimulation studies in TA1 and guide device development in TA2.

The recipient shall document the protocols for measuring monkey (b)(4) memory (b)(4) and shall train animals in the (b)(4) task. In parallel, the recipient shall conduct studies of the neurophysiology of stimulation (b)(4) .

The recipient shall then conduct behavioral studies of the electrophysiology (b)(4) in two monkeys. The recipient shall also perform a systematic study (b)(4) The recipient shall also probe the neurophysiology (b)(4)

3.1.16 Identifying neuronal basis of (b)(4) memory in NHPs and probing the role of stimulation (b)(4) (b)(4). This phase of the work seeks to characterize the patterns of neuronal activity that underlie (b)(4) memory in non-human primates. The recipient shall conduct (b)(4) recordings (b)(4).

3.1.16.1 The recipient shall design, program, and test experimental protocol for measuring monkey (b)(4) memory performance (b)(4) [Months 1-4].

(a) The recipient shall design and program a behavioral task for measuring monkey (b)(4) memory [Month 4].

3.1.16.2 The recipient shall document the hardware interface for the (b)(4) task to interface with recording equipment (b)(4) [Months 3-5].

(a) The recipient shall document the hardware/software interface for interfacing electrophysiological recordings, eye tracker, and monkey behavioral paradigm [Month 5].

3.1.16.3 The recipient shall train (b)(4) to (b)(4) perform the (b)(4) memory task [Months 5-24].

(a) The recipient shall obtain one monkey, complete pre-training health checks, place collars, complete quarantine and room acclimation procedures [Month 8].

(b) The recipient shall train the monkey in chairing and handling procedures, acclimate monkey to working in the laboratory, begin food delay procedures, train monkey on initial behavioral tasks, (b)(4) which will be used in the eye-tracking calibration procedure of the (b)(4) memory task [Month 10].

(c) The recipient shall train the animal in the (b)(4) memory paradigm [Month 24].

3.1.16.4 The recipient shall prepare monkey for recording and stimulation studies, including MRIs, surgeries to implant headposts and recording chambers, and craniotomies. The recipient shall conduct studies of neurophysiological correlates of monkey (b)(4) behavior without stimulation [Months 5-24] and shall:

(a) Perform pre-surgical MRIs on one monkey and perform surgery to implant headpost. Complete recovery from surgery [Month 12].

(b) Train one monkey on initial joystick task, including eye calibration and fixation training with head fixation via headpost [Month 15].

(c) Train monkey on the (b)(4) memory task, perform surgery to implant recording chamber [Month 18].

(d) The recipient shall document all findings in a final report [Month 19]

3.1.16.5 [DELETED]

3.1.17 Comprehensive examination of the electrophysiology of stimulation in non-human primates. (b)(4) (b)(4) study of the electrophysiology of stimulation. The recipient shall perform a systematic study of the ability for (b)(4) stimulation (b)(4) and identify (b)(4) parameters (b)(4). The recipient shall conduct both studies (b)(4) (b)(4).

3.1.17.1 The recipient shall prepare untrained monkeys for (b)(4) recording and stimulation studies (b)(4) (b)(4) . The recipient shall perform MRIs to guide electrode implantation, surgeries to implant headposts and recording chambers, and craniotomies.

(a) The recipient shall perform monkey surgeries to implant electrodes (b)(4) [Month 6].

3.1.17.2 The recipient shall demonstrate that neuronal stimulation (b)(4)

(a) The recipient shall show that (b)(4) stimulation (b)(4) [Month 9].

(b) The recipient shall document results of data analyses (b)(4) [Month 11].

(c) The recipient shall document all findings in a final report [Month 19]

3.1.17.3 [DELETED]

3.1.17.4 [DELETED]

3.1.17.5 [DELETED]

3.2 OPTION PERIOD (PHASE II)

Technical Area 1

3.2.1 Extending computational model (b)(4)

3.2.1.1 Modeling the dynamics of brain activity (b)(4)

(a) (b)(4) (b)(4) [Month 28]

(b) (b)(4) [Month 30]

(c) Formal report on the above milestones including code used to perform these analyses. [Month 36]

3.2.1.2 Using (b)(4) modeling to improve memory (b)(4) restoration:

(a) (b)(4) [Month 28]

(b) (b)(4)

(b)(4) . [Month 30]

(c) Final report on the use of (b)(4) modeling to improve memory (b)(4) (b)(4) restoration. [Month 36]

3.2.1.3 Incorporate (b)(4) modeling into (b)(4) algorithms:

(a) (b)(4) (b)(4) [Month 28]

(b) (b)(4) [Month 30].

(c) Deliver final report on the role (b)(4) across the various RAM tasks, and predicting which stimulation parameters are most likely to improve memory. [Month 34]

3.2.1.4 Using (b)(4) analysis to model memory:

(a) [Month 28]

(b) [Month 30]

(c) [Month 34]

(d) Final repor [Month 36]

3.2.1.5 Build a revised control algorithm strategy (b)(4)

(a) (b)(4) [Month 30]

(b) Complete a reanalysis of all parameter search (b)(4)

(b)(4)

[Month 34].

(c) Complete algorithm for (b)(4) selection of stimulation parameters during FR6 and CatFR6 tasks to maximize memory performance. [Month 43]

(d) Deliver a final report based on the above deliverables. [Month 48]

3.2.1.6 Collect high-resolution imaging and link (b)(4) models (b)(4) The recipient shall:

(a) Collect high-resolution magnetic resonance imaging sequences in 10 subjects, including T1/T2, diffusion and resting state functional scans. [Month 36]

(b) Collect high-resolution magnetic resonance imaging sequences in 50 subjects, including T1/T2, diffusion and resting state functional scans. [Month 42]

(c) Collect high-resolution magnetic resonance imaging sequences in 100 subjects, including T1/T2, diffusion and resting state functional scans. [Month 48]

(d) Deliver interim report on (b)(4) target selection (b)(4) predicted to reliably enhance (b)(4) memory (b)(4)

[Month 38]

(e) (b)(4)

[Month 41]

(f) Deliver interim report on the (b)(4) selection (b)(4) that reliably enhances (b)(4) memory (b)(4)

[Month 46]

(g) Final report on the efficacy of stimulation target selection based upon (b)(4) (b)(4) biomarkers in (b)(4) memory tasks. Report will include data from a minimum of 15 (b)(4) memory test sessions (e.g. FR6, CatFR6). [Month 48]

3.2.1.7 The recipient shall complete data collection in experiment FR1 and shall:

(a) Analyze data on 60 patients from experiment FR1 [Month 30].

(b) Analyze data on 66 patients from experiment FR1 [Month 36].

(c) Analyze data on 72 patients from experiment FR1 [Month 42].

(d) Analyze data on 78 patients from experiment FR1 [Month 48].

(e) Complete final reports on data from the above experiment, (b)(4) [Month 48].

(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.1.8 The recipient shall complete data collection in experiment CatFR1 and shall:

(a) Analyze data on 36 patients from experiment CatFR1 [Month 30].

(b) Analyze data on 38 patients from experiment CatFR1 [Month 36].

(c) Analyze data on 41 patients from experiment CatFR1 [Month 42].

(d) Analyze data on 43 patients from experiment CatFR1 [Month 48].

(e) Complete final reports on data from the above experiment, (b)(4) [Month 48].

(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

(h) Expand analysis functions (b)(4) [Month 30]

3.2.1.9 Design, program, pilot, execute, and analyze data from Experiment TH1. The recipient (b)(4) (b)(4) (b)(4) and shall:

(a) Deliver fully documented code and analysis functions [Month 26].

(b) Analyze data on 21 patients from experiment TH1 [Month 30].

(c) Analyze data on 32 patients from experiment TH1 [Month 36].

(d) DELETED

(e) DELETED

(f) DELETED

(g) DELETED

(h) DELETED

3.2.1.10 The recipient shall complete data collection and analysis in experiment PAL1 and shall:

(a) Analyze data on 31 patients from experiment PAL1 [Month 30].

(b) Analyze data on 36 patients from experiment PAL1 [Month 36].

(c) Analyze data on 42 patients from experiment PAL1 [Month 42].

(d) Analyze data on 47 patients from experiment PAL1 [Month 48].

(e) Complete final reports on data from the above experiment, (b)(4) (b)(4) [Month 48].

(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2 Stimulation to enhance (b)(4) memory

3.2.2.1 Continue to collect and analyze data from Experiment FR3. The recipient shall:

(a) Organize and annotate data from 19 patients [Month 36].

(b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].

(c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.2 Design, program, execute, and analyze data from Experiment PS4/FR5. (b)(4) The recipient shall:

(a) Deliver fully documented PS4/FR5 code and analysis functions [Month 32].
(b) Organize and annotate data from 6 PS4/FR5 patients [Month 36].
(c) Organize and annotate data from 9 PS4/FR5 patients [Month 43].
(d) Organize and annotate data from 29 PS4/FR5 patients [Month 48].
(e) Complete final reports on data from the PS4/FR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR3. [Month 48].
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.3 Design, program, execute, and analyze data from Experiment PS5/FR6. (b)(4) The recipient shall:

(a) Deliver fully documented PS5/FR6 code and analysis functions [Month 38].
(b) Organize and annotate data from 6 PS5/FR6 patients [Month 45].
(c) Organize and annotate data from 14 PS5/FR6 patients [Month 48].
(d) Complete final reports on data from the PS5/FR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in FR5. [Month 48].
(e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.4 [DELETED]

3.2.2.5 Continue to collect and analyze data from Experiment CatFR3. The recipient shall:

(a) Organize and annotate data from 10 patients [Month 36].
(b) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].
(c) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(d) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.6 Design, program, execute, and analyze data from Experiment PS4/CatFR5. (b)(4) The recipient shall:

(a) Deliver fully documented PS4/CatFR5code and analysis functions [Month 32].
(b) Organize and annotate data from 6 PS4/CatFR5 patients [Month 42].
(c) Organize and annotate data from 9 PS4/CatFR5 patients [Month 43].
(d) Organize and annotate data from 37 PS4/CatFR5 patients [Month 48].
(e) Complete final reports on data from the PS4/CatFR5 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in CatFR3 [Month 48].
(f) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(g) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.7 Design, program, execute, and analyze data from Experiment PS5/CatFR6. (b)(4) The recipient shall:

(a) Deliver fully documented PS5/CatFR6 code and analysis functions, (b)(4) [Month 38].

(b) Organize and annotate data from 6 PS5/CatFR6 patients [Month 45].

(c) Organize and annotate data from 23 PS5/CatFR6 patients [Month 48].

(d) Complete final reports on data from the PS5/CatFR6 experiment, including a report on the anatomical specificity of target selection, and a comparison with stimulation efficacy in CatFR5 [Month 48].

(e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.8 Design, program, execute, and analyze data from Experiment TH3. (b)(4) (b)(4) (b)(4). The recipient shall:

(a) Deliver fully documented code and analysis functions [Month 26].

(b) Organize and annotate data from 5 patients [Month 30].

(c) Organize and annotate data from 8 patients [Month 36].

(d) DELETED

(e) DELETED

(f) DELETED

3.2.2.9 DELETED

3.2.2.10 DELETED

3.2.2.11 Design, program, execute, and analyze data from Experiment PAL3. (b)(4) The recipient shall:

(a) Analyze data on 14 patients from the PAL3 experiment [Month 36].

(b) Analyze data on 14 patients from the PAL3 experiment [Month 42].

(c) Analyze data on 14 patients from the PAL3 experiment [Month 48].

(d) Complete final reports on data from the above experiment, including a report on the anatomical specificity of target selection [Month 48].

(e) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].

(f) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.12 Design, program, pilot, execute, and analyze data from Experiment PS4/PAL5. (b)(4) The recipient shall:

(a) Deliver fully documented PS4/PAL5 code and analysis functions [Month 32].

(b) Analyze data on 4 patients from the PS4/PAL5 experiment [Month 36].

(c) DELETED

(d) DELETED

(e) DELETED

(f) DELETED

(g) DELETED

3.2.2.13 DELETED

3.2.2.14 Continue to collect and analyze data from Experiments PS2. The recipient shall:

(a) Analyze data on 50 patients from experiments PS2 [Month 30].
(b) Analyze data on 71 patients from experiments PS2 [Month 36].
(c) Analyze data on 82 patients from experiments PS2 [Month 42].
(d) Analyze data on 93 patients from experiment PS2 [Month 48].
(e) Post fully annotated data to the public data portal for all patients run in the task [Month 48].

3.2.2.15. [DELETED]

3.2.2.16. [DELETED]

3.2.2.17. Design, program, execute, and analyze data from Experiment REC1. (b)(4) The recipient shall:

(a) Deliver fully documented code and analysis functions [Month 28].
(b) Organize and annotate data from 2 patients [Month 30].
(c) Organize and annotate data from 4 patients [Month 36].
(d) Organize and annotate data from 6 patients [Month 42].
(e) Organize and annotate data from 8 patients [Month 48].
(f) Complete final reports on data from the above experiment, (b)(4) [Month 48].
(g) Create 3D reconstructions of all patients run in the task in Phase 2 [Month 48].
(h) Post fully annotated data to the public data portal for all patients run in the task in Phase 2 [Month 48].

3.2.2.18 Enhance (b)(4) decoding capabilities

(a) Assess (b)(4) decoding performance within individual patients. For all patients who participated in the CatFR1 task, report (b)(4) accuracy and significance, and analyze (b)(4) to determine brain regions contributing to (b)(4) performance. [Month 43]
(b) Assess differences (b)(4) within individual patients. Assess (b)(4) to determine brain regions involved (b)(4) (i.e., significant regions). [Month 44]
(c) Develop a model to align neural features across patients (b)(4). Evaluate the ability of the model to predict brain activity from held-out patients. [Month 45]
(d) Using neural features aligned across patients, (b)(4) . [Month 46]
(e) Develop joint models (b)(4) . [Month 47]
(f) Final report on (b)(4) capability. Develop final report (b)(4) . Future research and development opportunities will also be identified. [Month 48]

3.2.3 Technology commercialization.

3.2.3.1 Develop implantable device concepts. Determine key risks and unknowns related to hardware development and identify strategies to reduce these risks. The recipient shall:

Establish preliminary requirements and specifications for the mechanical assembly of the implant, document the design intent and design the initial device concepts. Define the lead geometry and develop surgical placement guidance based on patient data collected as part of the RAM project. Complete an early feasibility analysis and cost

analysis of the identified device concept and a detailed project plan for subsequent development phases. [Month 44]

3.2.3.2 Develop device programmer prototype. (b)(4) The recipient shall:

(a) Develop implantable device simulator and API. (b)(4) [Month 45]

(b) Develop a graphical user interface (b)(4) [Month 46]

(c) Develop the patient testing module (b)(4) [Month 47]

3.2.3.3 Hold informational meeting with the FDA. The purpose of this meeting is to review Nia's product development roadmap with the FDA and obtain informal feedback from the FDA that can be used to guide future development efforts. Topics to be reviewed with the FDA include: Nia's concept of operations for the use of the technology in the home and the clinic, its mechanism of action, the patient populations that could benefit from our technology, and the outcome measures we propose to use to evaluate its therapeutic effect. The recipient shall:

(a) Submit an informational meeting request to the FDA [Month 46]
(b) Meet with the FDA to review Nia's development plans [Month 48]

3.2.3.4 Final report on technology commercialization activities. This report shall summarize progress on all of the commercialization activities, including the implantable device concepts, the programmer prototype and the informational meeting with the FDA. [Month 48]

3.2.4 Evaluate (b)(4) stimulation in patient cohort with a history of traumatic brain injury (TBI)

The recipient shall collect (b)(4) stimulation data from subjects with intractable epilepsy who undergo implantation of intracranial electrodes, with a focus on those with a prior history of traumatic brain injury (TBI). Each subject will undergo testing for at least five (5) sessions across three (3) task phases: 1) at least three (3) cognitive testing sessions to characterize biomarkers (b)(4) for (b)(4) stimulation; 2) at least one (1) session to search the parameter space (b)(4) and 3) at least one (1) session to evaluate (b)(4) stimulation (b)(4) for cognitive enhancement. Subjects will undergo high-resolution DTI scans and an in-depth analysis of their related medical history to allow for a characterization of the anatomical correlates of their TBI. For each subject, behavioral performance, EEG biomarkers, (b)(4) and data quality shall be characterized.

3.2.4.1 Collect and analyze record-only (b)(4) free recall data (FR1/catFR1) in patients with epilepsy and history of traumatic brain injury

(a) Test and report on 3 additional subjects with a prior history of traumatic brain injury on a record-only free recall task. [Month 57]
(b) Test and report on 6 additional subjects with a prior history of traumatic brain injury on a record-only free recall task. [Month 61]

3.2.4.2 Collect and analyze high-resolution diffusion imaging data and MRI-based brain volumetrics.

(a) Collect high-resolution diffusion imaging data for 3 subjects with prior history of TBI. Deliver interim report detailing imaging analyses characterizing each patient's history of traumatic brain injury. [Month 57]
(b) Collect high-resolution diffusion imaging data for 6 subjects with prior history of TBI. Deliver final report detailing imaging analyses characterizing each patient's history of traumatic brain injury. [Month 61]

3.2.4.3 Collect and analyze (b)(4) stimulation free recall data (FR5/catFR5) in patients with epilepsy and history of traumatic brain injury

(a) Test 3 additional subjects with a prior history of traumatic brain injury on a (b)(4) stimulation free

recall stimulation task (b)(4) [Month 57]

(b) Deliver interim report on (b)(4) stimulation. The report will include identification of biomarkers indicative of memory performance and a comparison of the TBI cohorts with non-TBI matched controls from the historical RAM dataset. [Month 57]

(c) Test 6 additional subjects with a prior history of traumatic brain injury on a (b)(4) stimulation free recall stimulation task (b)(4) [Month 61]

~~(a)~~(d) Deliver final report on (b)(4) stimulation in the TBI cohort, including data from the historical RAM dataset. [Month 61]

Technical Area 2

Phase 2 objectives in TA2 shall be to support FDA IDE approval and clinical site training, develop clinical systems, and (b)(4) Phase 1 algorithms.

3.2.4 Update system architecture and individual components based on TA1. The recipient shall review and, if necessary, redefine, document and review the high-level system design requirements for the (b)(4) system based on the discovery and feedback from TA1 in phase 1.

3.2.4.1 The recipient shall review and, if necessary, redefine system level specification with TA1 team based on the phase 1 results [Months 25–30].

3.2.4.2 The recipient shall review and, if necessary, redefine the specifications for neural interfaces [Months 25–30].

3.2.4.3 The recipient shall review and, if necessary, redefine the specifications for electronics including the stimulating and recording electronics [Months 25–30].

3.2.4.4 The recipient shall review and, if necessary, redefine the sub-chronic safety and performance data required by the FDA for 29-day IDE approval [Months 25–30].

3.2.4.5 The recipient shall produce a final set of documents detailing the specifications for the overall system and its components [Month 30].

3.2.5 Fabrication of the reusable (b)(4) stimulators for clinical studies. The recipient shall produce the balance of (b)(4) stimulator units for use at the clinical sites in early Phase 2.The recipient shall:

(a) Deliver ten tested and documented (b)(4) systems [Month 26].

(b) Deliver an additional thirty tested and documented (b)(4) systems [Month 30].

(c) Deliver an updated development plan, requirements, and design history file and limited verification and validation activities to cover the system integration with the (b)(4) Lead and (b)(4) splitter cable [Months 30].

(d) Utilize the (b)(4) to perform recording and closed-loop stimulation during memory testing in at least 50 patients [Month 48].

3.2.6 Evaluation of commercially available (b)(4) leads for memory enhancement. The recipient shall:

(a) Develop protocol amendment and obtain IRB approval to implant commercially-available leads (b)(4) (b)(4) in study patients [Months 34].

(b) Deliver interim report on memory (b)(4) performance in 10 subjects (b)(4) [Months 41].

(c) Develop protocol amendment and obtain IRB approval to implant commercially-available leads (b)(4) (b)(4) [Months 40].

(d) Deliver interim report on stimulation target localization in 10 subjects implanted (b)(4) [Months 44].

(e) Final report on memory (b)(4) performance and target localization in 40 subjects with (b)(4) leads [Month 48].

3.2.7 Algorithm prototyping system: (b)(4) algorithm development from TA1, Phase 1. The recipient shall document the development of a tool to (b)(4) successful TA1 algorithms (b)(4).

3.2.7.1 The recipient shall document the development of a (b)(4) tool to translate existing algorithms from phase 1 (b)(4) Months 33–42].

3.2.7.2 The recipient shall document the development of a tool (b)(4) [Months 33–42].

3.2.7.3 The recipient shall administer embedded-mode, closed-loop memory testing in the Epilepsy Monitoring Unit:

(a) Complete software tool for loading (b)(4) [Month 42].

(b) Complete software tool for translating software algorithm (b)(4) [Month 42].

(c) Administer (b)(4) memory task to five patients (b)(4). [Month 48]

3.2.8 [DELETED]

3.2.9 Core project resources devoted to TA2: (b)(4) algorithms, computational cluster equipment and administration, integration between TA1, TA2, and TA3 modeling and electrophysiology shall be documented.

Technical Area 3

[DELETED]

3.3 PROGRAM MANAGEMENT AND REVIEW

The Government will actively monitor, review and approve the recipient's performance to ensure all the performers are in sync and matched with the Government's requirements. The Government will ensure that each of the performers share experimental data across the program and will further ensure that the performers develop techniques and capabilities that are compatible and integrate with each other. The recipient shall collaborate and cooperate with other performers in the program under the coordination of the Government team. At Government PI meetings, the recipient shall demonstrate technical capabilities and engage and/or challenge other performers in a cooperative and challenge environment. Along these lines, the Government will ensure that each performer shares technical information with the others to enable the testing/challenging of each other's capabilities. The Government will further oversee the program and will review, approve, and participate in the demonstrations.

3.3.1 Kick-off Meeting

The recipient shall hold a kick off meeting within 60 days of award of this agreement. In this meeting, the recipient shall present a program management plan and financial tracking plan.

3.3.2 Quarterly Financial Reports

The recipient shall provide quarterly financial progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to provide a brief project progress and inform the GTR and Program Manager of any potential issues.

3.3.3 Quarterly Technical Reporting
The recipient shall provide quarterly progress reports to the Government Technical Representative (GTR) and DARPA Program Manager. The purpose of these reports is to present a summary of work completed by SOW tasking and milestones met, discuss any problems encountered, update the program schedule, present the program financial status, and discuss remaining work. Quarterly reports shall also include all technical data items generated including but not limited to experimental data, processed data along with methods of processing used, research reports and publications and software (source code and executables).

3.3.4 Monthly Status Reports
The recipient shall provide monthly status reports which will include all relevant project data including, but not limited to, raw and analyzed electrophysiological signals as well as any necessary annotations and interpretations of the data, such as time-stamped patient behaviors, necessary for appropriate analyses and interpretation of the data. Patient data shall be provided in a coded format that protects patient identities but will contain diagnosis (signs/symptoms), interventions including system modifications, technical observations, diagnostic tests/results, and patient outcomes. In addition, information about the device delivering therapy including device serial numbers, device model numbers, date of event, and country/state of event shall be annotated with the data and therapy. This data shall be made available on database accessible across the program and to Government personnel.

3.3.5 Final Agreement Review
The recipient shall host a final agreement review. The purpose of this review is to present a summary of all work completed and milestones accomplished and to discuss any relevant future efforts similar to the contract, which may be pursued. This report shall be provided to the Government Technical Representative (GTR) and DARPA Program Manager. A final summary report shall be provided at the end of the program.

3.3.6 System Development Plan (SDP)
The recipient shall describe the scope of the design and development effort, describe hardware, software architectures and experimental procedures (as applicable) in sufficient detail for review and replication, reference any applicable documents and provide a schedule. The recipient shall share the SDP with the other program performers and the Government.

3.3.7 System Documentation
The recipient shall provide system documentation documenting the source code, protocol and algorithm analysis, hardware description, format specifications, system diagrams, part numbers, and any other data necessary to replicate and test the designs.

4.0 INCIDENTAL HARDWARE AND SOFTWARE
Hardware and software incidental to this research shall be made available to the Government.

5.0 REPORTS AND PRESENTATION MATERIALS
The reports and presentation materials shall be delivered as described in the data matrix.

6.0 TRAVEL
Long distance domestic travel is estimated for Program Review meetings and Conferences.

7.0 PLACE OF PERFORMANCE
University of Pennsylvania
3401 Walnut St, Suite 302C
Philadelphia, PA 19104
Ph: 215-746-3501, Fax: 215-746-6848
kahana@psych.upenn.edu